Annals of Clinical and Analytical Medicine
Case Report

Sarcomatoid urothelial carcinoma accompanied by elevated serum β-HCG: Two case reports

Sarcomatoid urothelial carcinoma with elevated serum β-HCG

Sena Ece Davarcı[1], Hacer Demir[1], Arif Demirbaş[2], Gülsüm Şeyma Yalçın[3], Çiğdem Özdemir[4], Esra Özgül[5], Meltem Baykara[1]
[1] Department of Medical Oncology, Afyonkarahisar University of Health Sciences, Afyonkarahisar
[2] Department of Urology, Doruk Hospital, Bursa
[3] Department of Pathology, Afyonkarahisar State Hospital, Afyonkarahisar
[4] Department of Pathology, Afyonkarahisar University of Health Sciences, Afyonkarahisar
[5] Department of Radiology, Afyonkarahisar University of Health Sciences, Afyonkarahisar, Turkey

Abstract
Sarcomatoid urothelial carcinoma is a rare and aggressive variant. Serum β-hCG levels are used as a tumor marker in gestational trophoblastic diseases and germ cell tumors, but may also be elevated in high-grade bladder cancers. Here, we report two urothelial carcinoma cases with sarcomatoid differentiation that relapsed early after surgery with elevated serum β-hCG levels. The first case was a 65-year-old female and the second case was a 67-year-old man with sarcomatoid urothelial carcinoma located in the ureter and renal pelvicalyceal system, both of them relapsed with elevated β-hCG serum level to 146.8 mIU/mL and 242 mIU/mL, respectively. They died a few months after initial diagnosis; 4.9 and 2.5 months respectively.
Both sarcomatoid variant and β-hCG expression were associated with poor prognosis and advanced stage. However, β-hCG is not used as a tumor marker in urinary tract cancers yet, and its relationship with variant pathologies has not been clarified. We need multi-centered studies to reveal this relationship.

Keywords
β-HCG, Sarcomatoid Variant, Urothelial Carcinoma

DOI: 10.4328/ACAM.21473 Received: 2022-11-02 Accepted: 2022-12-31 Published Online: 2023-01-30 Printed: 2023-03-25 Ann Clin Anal Med 2023;14(Suppl 1):S112-115
Corresponding Author: Sena Ece Davarcı, Faculty of Health Science, Afyonkarahisar University, Afyonkarahisar, Turkey.
E-mail: beyaaz3@hotmail.com P: +90 555 222 33 54
Corresponding Author ORCID ID: https://orcid.org/0000-0003-1142-9411

Introduction

Sarcomatoid urothelial carcinoma is a rare and aggressive variant, which is thought to constitute approximately 0.3% of all urothelial carcinomas [1]. It is mostly located in the bladder and shows both epithelial and mesenchymal differentiation. Ureter and renal pelvis localizations are seen more rarely [2].

Human chorionic gonadotropin (hCG) is a glycoprotein that is secreted from the trophoblastic cells during pregnancy. Serum β-hCG levels are used as a tumor marker in gestational trophoblastic diseases and germ cell tumors, they can also elevate in high-grade bladder cancers and are associated with a poor prognosis [3]. Due to its rarity, we aimed to share two rare cases of urothelial carcinoma, which are accompanied with elevated β-hCG and show sarcomatoid differentiation.

Case Report

Case 1: A 65-year-old female patient applied to the Urology Department with macroscopic hematuria in June 2020. Abdominal MRI detected a 19x30x22 mm mass lesion in the left lateral wall of the bladder. Transurethral resection was performed and she was diagnosed with high-grade urothelial carcinoma with muscle invasion. The pathology result of radical cystectomy + ilioinguinal lymph node dissection surgery did not include immunohistochemical findings, and the pathological stage was pT2bN0. Post-operative abdominal MRI showed a lesion in the left lateral wall of the pelvis, which might be consistent with a 64x18 mm hematoma/lymphocele and a follow-up of the lesion was planned. Postoperatively, adjuvant cisplatin-gemcitabine chemotherapy was initiated on day 44. After the third cycle, the patient tested positive for COVID-19 PCR test and was given home isolation. At the end of home isolation, the patient re-applied to the Urology Department again 27 days after the last chemotherapy with a complaint of abdominal swelling. Abdominal MRI showed lesions in the intra-abdominal region and pelvis, with the largest size being 93x83 mm, which may be consistent with several metastatic cystic implants. Mass excision was performed for pathological diagnostic purposes. Pathology results showed cytokeratin (+), keratin-7 focal (+), p63 diffuse (+), p40 (+), hCG focal (+), Ki-67: 60-70%, vimentin weak (+), CD10 focal (+), S-100 (-), keratin 5/6 (-), keratin-20 (-), which is similar to the initial urothelial carcinoma, but there were regions showing focal sarcomatoid differentiation (Figure 1a and 1b). The pre-operative serum β-hCG level of the patient was 146.8 mIU/mL and postoperative serum β-hCG level regressed to 46 mIU/mL. In the post-operative period, the patient was hospitalized for maintenance therapy before initiation of the next line of chemotherapy, and we determined that her β-hCG level was elevated to 353 mIU/mL. Control abdominal MRI (Figure 1c, 1d and 1e) showed that the intra-abdominal implants had significantly progressed compared to the MRI taken 21 days ago. The chemotherapy could not be initiated because of the rapid deterioration of the general condition of the patient and she died 4.9 months after the first operation.

Case 2: A 67-year-old male patient applied to the Urology Department in September 2020 with right flank pain. In the abdominal USG, grade 4 dilatation in the right kidney and the right ureter was observed. Abdominal CT showed increased nodular thickness in the right pelvicalyceal system and irregularity in the wall along the course of the distal ureter with dilatation in the right ureter, the patient underwent a right nephroureterectomy operation. Pathology results showed a high-grade urothelial carcinoma with sarcomatoid differentiation located in the ureter and renal pelvicalyceal system, and cytokeratin (+) in epithelial component, keratin-7 (+) in the epithelial component, p53 20-30% (+) in the epithelial area, S-100 (-), ACTIN (-), Desmin (-), Vimentin (-), keratin-20 (-), CD34 (-), CD10 (-), EMA (-), and CD99 (-) (Figure 2a, 2b, 2c and 2d). The pathological stage was pT3N1. The abdominal CT performed on post-operative day 36 for baseline evaluation before the adjuvant chemotherapy showed high-density fluids and soft tissues along the ureter trace on the right, which cannot be clearly delineated from iliopsoas muscle. Since residue and hemorrhage could not be distinguished, an abdominal MRI was planned. Meanwhile, the patient applied to the Emergency Room on post-operative day 61 due to severe abdominal pain and he was hospitalized

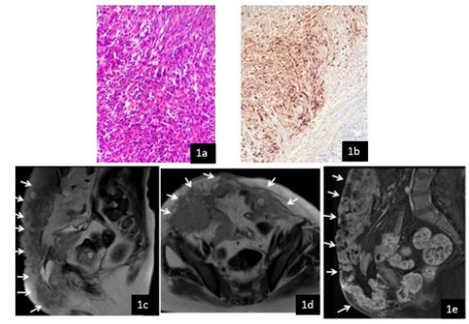

Figure 1. (1a) Staining with Hematoxylin and Eosin, (1b) Staining with β-hCG, (1c) Sagittal and (1d) Axial in T2-weighted sequences, multiple implants are seen on the anterior abdominal wall, extending to the intra-abdominal distance, and merging with each other. (1e) In the post- contrast sagittal fat-suppressed T1-weighted sequence, it is observed that the implants retain diffuse heterogeneous contrast.

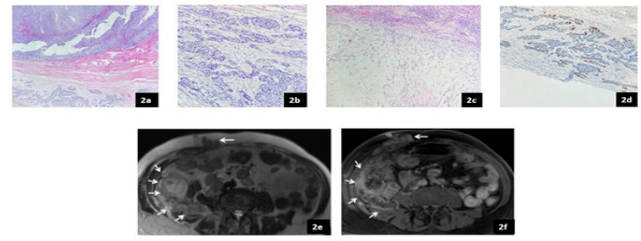

Figure 2. (2a) Urothelial component that fills the ureteral lumen and causes infiltration in the muscle layer (x40HE); (2b) Component infiltration of urothelial carcinoma in the ureteral wall (x200); (2c) Tumor component infiltrating the kidney parenchyma and showing sarcomatous differentiation (x100 HE) and (2d) Beta-HCG positive cell populations as focal foci in the area of urothelial carcinoma (X100). In axial T2 (2e) and post contrast fat-suppressed T1 (2f)-weighted sequences, implants with heterogeneous intensity on T2-weighted sequences in the right retroperitoneal region and anterior abdominal wall, and diffuse heterogeneous contrast enhancement after intravenous contrast material are observed.

at the Oncology Service due to acute renal failure. His β-hCG was measured at 242 mIU/mL. Patient's pre-operative β-hCG value had not been measured. Abdominal MRI showed a lesion with the size of 78x84x147 mm, with hemorrhagic intensities, starting from the sub-hepatic region in the right renal lodge, filling the entire retroperitoneal region, and extending to the iliacus muscle. It was found that the lesion infiltrated the right liver lobe, all segments of the iliacus muscle, and the posterior fibers of the psoas muscle and extended to the paraaortic area by pushing the inferior vena cava anteriorly (Figure 2e and 2f). Patient received hemodialysis after developing metabolic acidosis and hyperkalemia. However, patient's renal function tests did not improve, his general condition deteriorated rapidly, and he died 2.5 months after the first operation.

Discussion

Approximately 75% of urothelial carcinomas consist of pure urothelial carcinomas, while the remaining 25% are histological variants. The sarcomatoid variant constitutes 0.3% of all urothelial carcinomas [1, 4]. Sarcomatoid urothelial carcinoma located in the renal pelvis and/or the ureter is extremely rare, with less than 30 reported cases [2, 5]. Variant histology is important as it determines the risk, shows the prognosis, and can directly impact the treatment [1].

Gu et al. showed that sarcomatoid urothelial carcinomas are associated with more advanced disease and T stage [4]. Also, it is associated with poorer survival data when compared with classical urothelial carcinoma, and upper urinary system ureteral sarcomatoid urothelial carcinoma has the poorest prognosis that the lifespan of these cases does not exceed 1 year [4, 5].

In the study by Douglas et al. investigating the effect of serum β-hCG levels on prognosis in 235 patients diagnosed with urothelial carcinoma, the median survival was worse in the groups with higher β-hCG levels before and after neoadjuvant chemotherapy (18.6 months vs. 4.2 months, respectively) compared to those with lower β-hCG levels (NR vs. 42.7 months respectively). Moreover, in patients with N_{1-3} or M_1 disease diagnosed for the first time or patients who received another chemotherapy following relapse after previous peri-operative chemotherapy, high pre-treatment and post-treatment β-hCG levels were associated with reduced survival (median 8.6 months vs. 8.4 months, respectively) [3].

Dexeus et al. recommend measuring β-hCG levels prior to chemotherapy in advanced urothelial carcinomas. If the β-hCG level is above 50% of the normal value, regular measurement should be performed as it is a reliable marker for tumor response and progression [6]. Dobrowolski et al. have measured serum β-hCG levels of 79 bladder cancer patients before and 7 days after TUR. They showed that the mean serum β-hCG levels increased with increasing degrees of anaplasia and stage. They stated that the measurement of serum β-hCG levels is a good marker for differentiating superficial and deep tumors [7].

Venyo et al. reported elevated serum β-hCG levels with increasing histological grade. In addition, immunohistochemically, the frequency of β-hCG expression increases in correlation with grade and T stage. In patients with positive staining with β-hCG, recurrence occurs with higher grade and stage [8]. Compatible with the literature, our two cases were high-grade and showed both elevated serum β-hCG levels and β-hCG expression in IHC. In the first case, adjuvant chemotherapy was initiated after radical cystectomy, but the patient had an early relapse and died 4.9 months after the first operation. The second case, in a rare way, was diagnosed with sarcomatoid urothelial carcinoma located in the renal pelvis and the ureter and presented with recurrence before adjuvant chemotherapy was initiated and died 2.5 months after the operation. The aggressive course of these two cases supports that the sarcomatoid variant and serum β-hCG elevation and IHC expression are associated with poorer survival.

Unfortunately, the serum β-hCG levels were not measured before the operation in the second case. However, with elevated serum β-hCG, β-hCG staining was demonstrated in the tumor tissue immunohistochemically in both cases. In addition, the decrease in serum β-hCG levels after metastasis excision in the first case and its elevation after disease progression supports the studies suggesting that serum β-hCG levels may be associated with the mass amount and that its follow-up in patients with high levels may show the progression.

Conclusion

Due to the fact that sarcomatoid urothelial carcinoma is extremely rare, data in the literature are mostly single-center and retrospective, and include a small number of cases and case reports. In urothelial carcinomas, β-hCG levels can be measured in serum and urine and stained in IHC. However, β-hCG is not used as a tumor marker in urinary tract cancers yet, and its relationship with variant pathologies has not been clarified. Therefore, multi-center, prospective studies involving more patients and pathological variants are needed to demonstrate the importance of β-hCG expression.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

***Funding**: None*

References

1. Lobo N, Shariat SF, Guo CC, Fernandez MI, Kassouf W, Choudhury A, et al. What is the significance of variant histology in urothelial carcinoma? Eur Urol Focus. 2020;6(4):653-63.

2. Mohan BP, Jayalakshmy PL, Letha V, Bhat S. Sarcomatoid Carcinoma of Renal Pelvis Involving Ureter and Renal Parenchyma with Heterologous Osteosarcomatous Differentiation: A Case Report and Review of Literature. Iran J Pathol. 2018;13(1):89-93.

3. Douglas J, Sharp A, Chau C, Head J, Drake T, Wheather M, et al. Serum total hCGβ level is an independent prognostic factor in transitional cell carcinoma of the urothelial tract. Br J Cancer. 2014;110(7):1759-66.

4. Gu L, Ai Q, Cheng Q, Ma X, Wang B, Huang Q, et al. Sarcomatoid variant urothelial carcinoma of the bladder: a systematic review and meta-analysis of the clinicopathological features and survival outcomes. Cancer Cell Int. 2020;20(1):550.

5. Wang Y, Liu H, Wang P. Primary sarcomatoid urothelial carcinoma of the ureter: a case report and review of the literature. World J Surg Oncol. 2018;16(1):77.

6. Dexeus F, Logothetis C, Hossan E, Samuels ML. Carcinoembryonic Antigen and Beta-Human Chorionic Gonadotropin as Serum Markers for Advanced Urothelial Malignancies. J Urol 1986;136(2):403-7.
7. Dobrowolski ZF, Bryska B, Dolezal M. Prognostic Value of Beta Human Chorionic Gonadotrophin in Blood Serum of Patients with Urinary Bladder Tumors. Int Urol Nephrol. 1994;26(3):301-6.
8. Venyo AKG, Herring D, Greenwood H, Maloney DJL. The expression of Beta Human Chorionic Gonadotrophin (β-HCG) in human urothelial carcinoma. Pan Afr Med J. 2010; 7:20.

How to cite this article:
Sena Ece Davarcı, Hacer Demir, Arif Demirbaş, Gülsüm Şeyma Yalçın, Çiğdem Özdemir, Esra Özgül, Meltem Baykara. *Sarcomatoid urothelial carcinoma accompanied by elevated serum β-HCG: Two case reports. Ann Clin Anal Med 2023;14(Suppl 1):S112-115*